Application No.: 10/655,915 Response dated: April 30, 2007

Reply to Office Action dated: October 31, 2006

## **Amendments to the Specification:**

Please replace paragraph [00018] with the following re-amended paragraph:

[00018] The inventors thus proceeded to characterize the genes and sequences in the 7 Mb region. It was discovered that for each of the genes present, the alleles of the genes carried by the most severely diabetic mice was the same as the alleles of the genes carried by the less severely affected mice, with the sole exception of the allele of the SorCS1 gene. Fig. 1 illustrates a genetic map of the genetic elements found in the 7 Mb region associated with the genetic difference. The region between map units 55 and 48 carried the genetic difference. The alleles of the SorCS3 gene turned out to be identical in the two strains of mice. As illustrated in Table 1 below, however, the susceptible mice had an allele of the SorCS1 gene that is three nucleotides different from that of the less severely diabetic mice. The resulting protein is also three amino acids different. This difference results in a genetic susceptibility to type 2 diabetes.

TABLE 1
SorCS1 mutations altering amino acids

Nucleotide			Amino Acid			
position in cDNA	В6	BTBR	position in protein	В6	BTBR	_isoform(s)
172	C	Т	52	Thr	Ile	a,b,c
<u>3436</u> <del>3433</del>	C	T	<u>1140</u> <del>1139</del>	Ser	Phe	a
3465 3462	T	C	<u>1150</u> <del>1149</del>	Ser	Pro	С